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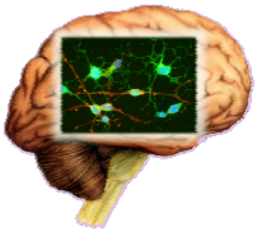
USUHS Neuroscience Newsletter



Neuroscience Welcomes Two New Students in 2007:
Omar Logue and Michael Davis

Omar Logue (left)
Michael Davis (right)

Omar Logue is originally from Vicksburg, Mississippi. He graduated with a B.S. in biology from Millsaps College, a liberal arts college in Jackson, Mississippi. In November 2006, he completed five years of active duty in the infantry by serving as a sergeant in the 82nd Airborne Division. Omar served three combat tours in Iraq. Recently, he worked as a laboratory technician for Innovative Biosensors, Inc., a local biotech firm that was awarded a government contract to create and install a pathogen detection system for the Pentagon Force Protection Agency (PFPA). As a member of the research and development team, he visited and collaborated with the PFPA scientists at the Pentagon to plan the implementation of the pathogen detection system. He and his wife, Charlene, were married in May 2007. He wants his research to focus on the mutations that occur in the regulatory proteins that control apotosis in neural cells, and their neurodegenerative roles in Alzheimer's and Parkinson's diseases.

Michael Davis is from San Diego, California. He obtained his BS in Biological Sciences from UC Riverside in 2004. During his undergraduate years he performed research on the effects of cigarette smoke in causing apoptosis of endothelial cells as the initiator of atherosclerosis. He then worked in the biomedical industry for three years focusing on medical diagnostic assays as a chemist. During his time as a chemist he also obtained an EMT license and worked as a private tutor. Michael's interests in neuroscience are focused on sensory and motor prosthetic/neural interfaces, brain/machine interfaces and neural regeneration. His hobbies are ocean swimming, bicycling, and running.

THE NEUROSCIENCE PROGRAM – "WHO ARE WE?"

Of course, the students are the core of our program. Who is actually teaching and mentoring our students? The lists below are acknowledgements to the many faculty, and students too, who have had formal roles interacting with students over the last year in the activities of the neuroscience curriculum. The number of people involved is always somewhat surprising, but much appreciated!!

MS. TINA FINLEY: HELPS WITH ALL OUR COURSES AND ACTIVITIES!

INTRODUCTION TO NEUROSCIENCE

Course Director: John Wu Co-Director: Richard Siarey
Graduate Student Assistants: Jeremy Henriques, Amy Starosciak
Organizer/Advisor for Oral Presentations: Mike Schell
Oral Presentation Judges: Kris Heitman, Gudrun Ihrke
Formal Lecturers: Sharon Juliano; Xiang Yao, Tyler Best, Regina Armstrong, Yu-min Zhang, Sue Bausch, Zygmunt Galdzicki, Richard Siarey, Tom Cote, Martin Doughty, Martha Johnson, Deb McLaughlin, Tim O'Neill, Howard Bryant, Joe McCabe, Greg Mueller, Brenda Elliott, Jennifer Schiltz, Neil Grunberg
Grading of Student Papers: Steve Rothwell, Cathy Jozwik, Leslie McKinney, Patty Deuster, Jennifer Schiltz, Sharon Juliano, Richard Siarey
Guided Students on Papers: Regina Armstrong, Diane Borst, Maria Braga, Tom Darling, Martin Doughty, Neil Grunberg, Jennifer Schiltz, Yumin Zhang
Exam Preparation: Jeremy Henriques, Amy Starosciak, Danette Cruthirds, Nicole Flint

ADVANCED TOPICS AND TECHNIQUES IN NEUROSCIENCE

Course Director: John Wu
Dr. Neil Grunberg was instrumental in setting the stage for the use of the text book, "Experimental Design for Biologists". In doing so, he gave two lectures, connect the lectures between modules and with the Introduction to Neuroscience course, and also ran the oral presentation component of the course. His energy and love for teaching/learning is infectious!
Presenters for Lectures and Demonstrations: Juanita Anders, Vassiliki Aroniadou-Anderjaska, Regina Armstrong, Thomas Baginski, Maria Braga,Tyler Best, Diane Borst, Martin Doughty, William Driscoll, Brita Fritsch. Zygmunt Galdzicki, Neil Grunberg, David Jacobowitz, Catherine Jozwik, Lara Kingeter, Greg Mueller, Steve Rothwell, Brian Schaefer, Richard Siarey, James Smirnioto-

INTERACTIONS BETWEEN BEHAVIOR, NEUROBIOLOGY, AND ENVIRONMENT

Course Director: Martha Faraday
Dr. Faraday organized and led this course – coming to USU after completing her workday at NIH!

MOLECULAR BASIS OF NERVOUS SYSTEM FUNCTION

Co-Course Directors: Sharon Juliano and Aviva Symes
Discussion Leaders: Aviva Symes, Regina Armstrong, Yumin Zhang, Zygmunt Galdzicki, Marcin Gierdalski, Sylvie Poluch, Denes Agoston, Tarik Haydar, Sharon Juliano

NEUROSCIENCE SEMINAR

Course Director: Tim O'Neill
Dr. Tim O'Neill covers the big picture for the series and works with Tina Finley to handle the logistics - but the success of the seminar series is dependent upon everyone's participation, most especially the many faculty members who volunteer to host speakers, meet with speakers, and attend seminars. Similarly, the student participation in the lunch meetings and seminar contributes to a productive visit for each speaker.

NEUROBIOLOGY OF DISEASE

This course was run by Dr. Ajay Verma for many years and with his departure we had some big shoes to fill on short notice to make this course possible with leadership from within our Neurology Dept and help from many outside invited lecturers.
Course Director: Jack Tsao
Oral Presentation Grading: Ann Marini

INTRODUCTION TO DEVELOPMENTAL NEUROBIOLOGY

This course is offered in alternate years from the Neurobiology of Disease course and so was held in 2006 and will be offered again in 2008.
Course Director: Sharon Juliano
Formal Lecturers: Regina Armstrong, Martha Johnson, Joshua Corbin, James Coulombe, Denes Agoston, Sharon Juliano, Michael Schell, Diane Borst, Martin Doughty

INTRODUCTION TO RESEARCH IN NEUROSCIENCE

Course Director: Regina Armstrong

NEUROSCIENCE TUTORIAL

Course Director: Regina Armstrong

NEUROSCIENCE ROTATIONS (2006-2007 academic year)

Rotation Advisors: Jennifer Schiltz, Ann Marini, Maria Braga, Jack Tsao, Greg Mueller, Yumin Zhang, Regina Armstrong, Sharon Juliano, Aviva Symes, Martin Doughty, Ying-Hong Feng, Tim O'Neill, Ajay Verma, Diane Borst, Zygmunt Galdzicki, John Wu, Maria Braga, Patty Deuster

Required classes in our Neuroscience curriculum also include classes that utilize the medical school lectures.

MEMBRANE AND ENDOCRINE PHYSIOLOGY
Course Director: Howard Bryant Co-Director: Greg Mueller

CLINICAL HEAD & NECK AND FUNCTIONAL NEUROSCIENCE
Course Director: Rosemary Borke

PRINCIPLES OF PHARMACOLOGY; NEUROPHARMACOLOGY
Course Directors: Brian Cox; Tom Cote

These classes are not Neuroscience courses like the others being acknowledged here, but, there are separate organizational, testing, and mentoring issues that must be handled for the Neuroscience students to function within a medical school course.

In addition to the faculty involved in courses and rotations, we also assign temporary advisors for each first year student (until they pick a thesis lab after the final rotation).
Temporary Advisors (2006-2007 academic year): Ann Marini, Aviva Symes, Maria Braga, Diane Borst, Jennifer Schiltz, Regina Armstrong

And finally, what could be more work for the second year students than a course???

QUALIFYING EXAMS!!!

Committee Chairs: Joe McCabe, Juanita Anders, Aviva Symes, Denes Agoston, Sue Bausch, Greg Mueller
Committee Members: Jennifer Schiltz, Tim O'Neill, Sue Bausch, Joe McCabe, Sharon Juliano, Martin Doughty, Ying-Hong Feng, He Li, Mike Schell, Yumin Zhang, Lei Zhang, Diane Borst, Regina Armstrong, Maria Braga, Aaryan Namboodiri, Fabio Leonessa, Ann Marini, Xiang Yao, Neil Grunberg, John Wu.

But wait! The thesis is still to come – THESIS ADVISORY COMMITTEES

Thesis Advisors: Joe McCabe, Sharon Juliano, Regina Armstrong, Juanita Anders, Denes Agoston, John Wu, Sue Bausch, Mike Schell, Aviva Symes, Maria Braga, Zygmunt Galdzicki, Tim O'Neill, Ajay Verma, Yumin Zhang, Neil Grunberg
Committee Members: (some listed as advisors are also committee members for additional students but not listed again) Nelson Arispe (APG), Stephano Vicini, Tom Cote, Regina Day , Robert Handa, Michael Schamblott, David Jacobowitz, Diane Borst, Lee Poth, Seibel Day, Jay Thackar, Tom Darling, Geoff Ling, Scott Young, Marylou Cutler, Ludise Malkova.

NEUROSCIENCE GRANT APPLICATIONS: DID YOU KNOW?

Among the neuroscience faculty members at USU, we have an informal mechanism for those who want to get some input from others while preparing a grant application. Dr. Kaminsky and Dr. Armstrong try to facilitate interactions among the faculty. If you have a section of your grant prepared, maybe just a Specific Aims page, you can send it to us with any information you want to communicate for your desired feedback (e.g. particular topic or technique expertise). We will then try to read your material and identify several other faculty members who will be invited to comment. If appropriate, Dr. Kaminsky and I will provide comments as well.

The review comments will all be through a direct interaction with the principal investigator (PI). The comments may be just notes written right onto the grant draft with subsequent discussion between the reviewer and PI to clarify. Those invited to review do not have to put effort into the writing of a review. This face-to-face discussion is expected to be non-judgmental and focus on constructive comments to improve the application.

As you may have inferred by terms like “invited”, this is an all-volunteer effort among those willing to participate. Through this collegiality, those who review for others should learn from the process as well as potentially have someone willing to review for them in the future.

For this interaction to function, the PI needs to provide a draft and allow sufficient time for others to comment. A Specific Aims page may take a turn-around time of a couple of weeks. Proportionally more time should be allowed for comments on longer text. The PI should continue to progress in preparing the application while the text is being distributed for comment. “Fast Track” applications cannot be accommodated. As with review of all grants, the faculty members involved will be required to keep the information confidential.

Several faculty members have already worked through this submission and feedback process. Thank you to those who have already helped this work. The “success” of the comment process will be variable for each application but the overall result should be that discussion of ideas is better than writing in a vacuum. Of course, as always, each PI is encouraged to take advantage of any expert contacts that are willing to provide confidential comments whether at USU or elsewhere.

Please email Dr. Steve Kaminsky or Dr. Regina Armstrong with any questions, concerns, or materials for review.

NEUROSCIENCE SEMINAR SCHEDULE 07/08

SEMINARS IN ***LECTURE ROOM A*** on ***WEDNESDAYS*** at ***3:30PM*** (subject to changes)

September 5, 2007
John Isaac
National Institute of Neurological Disorders and Stroke

September 19, 2007
John H McDonough
Pharmacology Branch
US Army Med Res Inst Chem Def

October 3, 2007
TBD

October 17, 2007
Jacqueline N. Crawley
National Institute of Mental Health

November 14, 2007
Neuroscience Open House

January 16, 2008
Raymond C. Koehler
Department of Anesthesiology
Johns Hopkins University

February 13, 2008
Juan M. Saavedra
National Institute of Mental Health

February 27, 2008
Joseph G. Verbalis
Department of Medicine
Georgetown University Medical Center

March 12, 2008
Thaddeus S. Nowak, Jr.
University of Tennessee Health Science Center, Memphis

April 16, 2008
Jack M. Parent
Department of Neurology
University of Michigan Medical Center

April 23, 2007
Jeffery L Barker
National Institute of Neurological Disorders and Stroke

The Neuroscience Program has the following DVD (or VHS format) resources that can be signed out through Tina Finley.

Video Textbook of Neurology for the Practicing Physician (Martin Samuels, MD):

1. The Neurological Exam
2. Functional Neuroanatomy
3. Peripheral Neuropathy
4. Degenerating and Demyelinating Diseases
5. Stroke
6. Seizures
7. Coma and Other Abnormalities of Consciousness
8. Headaches

Biology and Human Behavior: The Neurological Origins of Individuality, 2nd Edition
Robert Sapolsky, PhD, Stanford University

Argumentation: The Study of Effective Reasoning, 2nd Edition
David Zarefsy, PhD, Northwestern University

ABSTRACT
"EFFECT OF TRAUMATIC STRESS ON MULTIPLE AMINERGIC SYSTEMS IN AMYGDALA AND HYPOTHALAMUS: SPECIFIC IMPAIRMENT OF 5-HT_{2A} RECEPTOR SIGNALING AND ITS PATHOPHYSIOLOGICAL ROLE IN AN ANIMAL MODEL OF POST-TRAUMATIC STRESS DISORDER"

Xiaolong Jiang, Ph.D.
Thesis Directed By: He Li MD., Ph.D. Associate Professor, Department of Psychiatry

The amygdala and hypothalamus are central brain regions participating in stress response. This response also requires participation of multiple aminergic systems, which extensively interconnect with the amygdala and hypothalamus. Thus, dysregulation of aminergic systems, particularly the serotonergic and noradrenergic systems, is closely linked with multiple anxiety and stress disorders. The present study, utilizing a learned helplessness stress model, determined if alterations of aminergic systems in the amygdala and hypothalamus were involved in stress-induced behavioral and physiological abnormalities associated with anxiety and stress disorders.

The principle electrophysiological function of serotonergic, histaminergic and noradrenergic systems in the basolateral amygdala (BLA) was to suppress excitability of the BLA by facilitating BLA GABA release (for serotonin) exposed to three-day restraint/tail shock, or decreasing glutamate release (for histamine and norepinephrine). These actions were primarily mediated by the 5-HT_{2A} receptor, histamine H_3 receptors, and α_2 adrenoceptor respectively. In rats 5-HT_{2A} receptor-mediated serotonergic facilitation of GABA release was severely impaired, while α_2 adrenoceptor-mediated and H_3 receptor mediated action in the BLA were not significantly changed. Quantitative RT-PCR and western blot analysis further demonstrated that stress specifically downregulated BLA 5-HT_{2A} receptors, without affecting other aminergic receptors. In addition, treatment with the selective 5-HT_{2A} receptor antagonist, MDL 11,939 during stress, which would prevent amygdala 5-HT_{2A} receptor downregulation, prevented the occurrence of enhanced acoustic startle response (ASR), a stress-induced behavioral manifestation that depends on the amygdala.

Since serotonin in the hypothalamus provides an important mechanism mediating feeding and body weight, the present study also examined whether sustained body weight loss in stressed animals is associated with dysregulation of hypothalamic serotonergic system. Stress downregulated the hypothalamic 5-HT_{2A} receptor, while other serotonergic receptor such as 5-HT_{2C} and 5-HT_{1A} receptor remained unchanged. Pretreatment with the selective 5-HT_{2A} antagonist, MDL 11,939, which would prevent stress-induced downregulation of hypothalamic 5-HT_{2A} receptors, dose-dependently reversed sustained body weight loss in stressed animals.

These findings indicate that BLA and hypothalamic 5-HT_{2A} receptors, but not H_3 receptor, α_2 adrenoceptor and other serotonin receptors, play a critical role in pathophysiological response to traumatic stress, and alteration of this receptor in the BLA and hypothalamus may represent an essential mechanism underlying the emergence of behavioral and physiological abnormalities resulting from stress, such as enhanced ASR and sustained body weight loss. Hence, 5-HT_{2A} receptor ligands may be potential preventive or therapeutic agents for stress-associated psychiatric disorders, especially post-traumatic stress disorder.

ABSTRACT
"REPAIR OF NEOCORTEX IN A MOUSE MODEL OF CORTICAL DYSPLASIA"

Alisa W. Schaefer, "Ph.D."
Thesis Directed By: Sharon Juliano, Ph.D., Professor,
Department of Anatomy, Physiology, and Genetics

Our lab developed an animal model to elucidate factors associated with abnormal neocortical development and to attempt repair of cortical dysgenesis. We disrupt corticogenesis using an anti-mitotic methylazoxy methanol (MAM), which inhibits mitosis for several hours. The effects of MAM on neocortical development are assessed during early (embryonic day 24; E24) and late (E33) corticogenesis in ferrets. These animals have protracted cortical development with neurogenesis and migration continuing postnatally. MAM treatment on E24 leads to disorganized cortical laminae, abnormal radial morphology, precocious differentiation of radial glia, and dispersal of Cajal Retzius cells. MAM treatment on E33 leads to less severe effects including diminished layer 4, widespread termination of thalamocortical afferents, and abnormal distribution of $GABA_{A\alpha}$ receptors. Reelin is a protein that plays a role in cortical layering and may also be a key factor in radial alignment. To assess the role of reelin in migration and radial morphology in our model, organotypic cultures were paired with wild type, heterozygous, or reeler mouse cortex. We observed that although reelin is necessary for cortical migration, other factors in neocortex rescue radial morphology and reelin is not required for proper elongation of radial glia.

In attempts to repair E33 MAM treated cortex, we transplanted E27, E33 ferret and E14 mouse neural progenitor (NPs) cells into organotypic slices. Using a different paradigm, E27 and E33 fNPs were injected into the brains of E33 MAM treated and normal ferret kits. All donor cell types survive well in culture and differentiate into multiple cell phenotypes of neural origin. When transplanted into organotypic cultures, all donor cells survive and migrate into the cortical plate, although injections into the ventricular zone were significantly more likely to reach the cortical plate than transplants into the intermediate zone. *In vivo* transplants of fNPs into ferret kits also migrate into the cortex, differentiate, and become neurons, but not glia. The *in vivo* studies further revealed that the migration pattern of transplanted cells into MAM cortex varies from their distribution in normal cortex and that donor cells of different ages migrated into distinct layers in normal versus MAM cortex.

Your Graduate Student Representative

is currently Felicia Qashu.
Each USUHS graduate program has a Student Program Representative whose role is to serve as liaison between administration/faculty and graduate students through the dissemination of pertinent information. This position also allows students to raise concerns and issues that can then be addressed through more formal channels. If you have any questions, comments or concerns, please contact Felicia (frankin@usuhs.mil).

ABSTRACT
"EVALUATION OF THE ADULT GOLDFISH BRAIN AS A MODEL FOR THE STUDY OF PROGENITOR CELLS"

Tara B. Romanczyk, "Ph.D."
Thesis Directed By: Juanita Anders, Ph.D., Professor,
Department of Anatomy, Physiology, and Genetics

Our understanding of the cellular and molecular mechanisms underlying adult neurogenesis in response to diseases of the CNS is incomplete. Decreased neurogenesis in the adult hippocampus in response to stressors is well established in rodent and nonhuman primate models of depression. Recently, increased neurogenesis has been linked to the actions of certain antidepressants, including tranylcypromine (TCP) in the treatment of depression. The goldfish (*Carassius auratus*) has the ability to grow its body and brain throughout its life and is an ideal model for studying adult neurogenesis. The hypothesis was that alterations in adult goldfish proliferation zones can be used to determine antidepressant effects on proliferation. Three specific aims were used to test this hypothesis: 1) To produce an atlas of the goldfish brain based on cresyl violet stained sections. 2) To construct an atlas of proliferation zones in the goldfish brain. 3) To study the influence of tranylcypromine on progenitor cell proliferation zones in the telencephalon, optic tectum, and cerebellum of adult goldfish.

Proliferation zones were identified using BrdU and H3 immunohistochemistry and mapped using the brain atlas. Proliferation zones were associated with periventricular surfaces in the telencephalon, diencephalon, optic tectal lobes, cerebellum, and hindbrain. The presence of proliferation zones within the hindbrain was one region that differed from other teleosts.

The effects of TCP on proliferating cells in the adult goldfish brain were examined. TCP caused a significant increase in cell proliferation in the optic tectum and cerebellum as detected by BrdU immunohistochemistry. Comparison of the treatment paradigms determined that short term TCP treatment caused significantly more proliferation than long term TCP treatment when examined at 16 hour BrdU administration. The significant decrease in BrdU labeled cells observed in the long term TCP treatment may be attributed to apoptosis, a process coupled with neurogenesis. These results demonstrate that the goldfish is as an excellent model for investigating the mechanisms involved in antidepressant effects on the brain.

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